Anti-inflammatory effects of rosiglitazone in patients with stage 4 and 5 chronic kidney disease

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON29938

Source
ToetsingOnline

Brief title
Hercules

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Renal disorders (excl nephropathies)

Synonym
chronic kidney disease, inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,GlaxoSmithKline

Intervention

Keyword: calcification, CKD(chronic kidney disease), inflammation, intima media thickness

Outcome measures

Primary outcome

The primary aim of this study will be to determine the effect of rosiglitazone

on intima media thickness and calcification

Secondary outcome

The secondary end points are the effects on the lipid profile, insulin

resistance, blood pressure and inflammation. The drug safety profile is

monitored by liver function parameters and weight changes and other adverse

events.

Study description

Background summary

Patients with renal disease are characterized by high morbidity and mortality due to complications of premature cardiovascular disease (CVD). The pathophysiological background of this excessive cardiovascular risk is not completely understood but multiple factors seem to be important. Classic risk factors such as dyslipidemia, hypertension and smoking are prevalent in patients with chronic kidney disease but are not sufficient alone to account for the high prevalence of CVD in this condition. It has been postulated that non-traditional risk factors, such as volume overload, inflammation and insulin resistance are important.
Thiazolidinediones (TZDs) or glitazones constitute a relatively new class of antihyperglycemic agents that improve insulin action in skeletal muscles, liver and adipose tissue, and thus decrease insulin resistance through activation of a nuclear receptor, the peroxisome proliferator-activated receptor gamma (PPARγ), which regulates the expression of genes controlling the synthesis of proteins that take part in glucose and lipid metabolism. TZDs are therefore currently used as antidiabetic drugs. Glucose intolerance is a nearly universal finding in patients with chronic renal failure and in animal models of uremia. The glucose intolerance results from impaired insulin-mediated glucose disposal

by muscle, adipose, and liver tissue. In type 2 diabetes patients, rosiglitazone appears to be effective in reducing pulse wave velocity (PWV). Whether these changes occur in advanced chronic kidney disease non-diabetic patients is currently unknown.

Study objective

The primary aim of this study will be to determine the effect of rosiglitazone on intima media thickness and calcification in patients with stage 4 and 5 CKD. The secondary end points are the effects on pulse wave velocity, blood pressure, the lipid profile, insulin resistance and inflammation.

Study design

This is a double blinded placebo controlled study in patients with stage 4 and 5 chronic kidney disease. Eligible patients in the outpatient kidney clinic will be informed by their treating physician about the study and they will be asked to join the study. Following informed consent the eligible patients will undergo baseline evaluation and will then be followed for a period of 48 weeks. A total of 200 non-diabetic stage 4 and 5 CKD patients will be evaluated at baseline..
The original medication will be continued. Fifteen patients will receive rosiglitazone 4 mg once per day for the initial 8 weeks and, after checking serum transaminases, the doses will be doubled for the remaining 4 weeks of the study. The other 15 patients form the control group. The total follow-up will be 48 weeks.

Intervention

100 patients will receive rosiglitazone 4 mg once per day for the initial 8 weeks and, after checking serum transaminases, the doses will be doubled for the remaining 4 weeks of the study. The other 100 patients form the control group

Study burden and risks

In clinical practice when rosiglitazone is administered to patients with diabetes the most commonly side effects (1-10%) are: edema,anemia and hypercholesteolemia. There are other side effects but this are relatively rare. In this study, it we closely monitor potential side effects.

Contacts

Public

Academisch Medisch Centrum

Albinusdreef 2
2300RC Leiden
Nederland
Scientific
Academisch Medisch Centrum

Albinusdreef 2
2300RC Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

CKD, stage 4 (GFR <30/min), predialysis

Exclusion criteria

heart failure (NIHA 3 or 4), elevated liver enzymes

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-09-2006
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	avandia
Generic name:	rosiglitazone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	15-06-2006
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-003001-49-NL
CCMO	NL12851.058.06